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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/076,900	02/14/2002	David B. Weiner	UPAP-0497	3962

34137 7590 11/21/2005

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EXAMINER	
LI, QIAN JANICE	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 11/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/076,900	WEINER ET AL.	
	Examiner	Art Unit	
	Q. Janice Li, M.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15,16,39-54,81-91 and 93-114* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15,16,39-43,45-49,51-53,81,83,85,87,89-91,93,95-97,99,101-103 and 108-114* is/are rejected.

7)☒ Claim(s) *44,50,54,82,84,86,88,94,98,100 and 104-107* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *2/23/05* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/18/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/23/05 has been entered.

Claim 15 has been amended. Claim 92 has been canceled. Claims 108-114 are newly added. Claims 15, 16, 39-54, 81-91, 93-114 are now pending in the application, and under current examination.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 15, 16, 39-41, 45-47, 51, 81, 83, 85, 87, 89, 93, 95, 99, 101, 108-114 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Carson et al* (US 5,679,647), in view of *Gately et al* (Cell Immunol 1992;143:127-42), and as evidenced by *Harris et al* (J Pharm Sci 1992;81:1-10).

Carson et al teach a method of inducing an immune response in an individual against an antigen by intranasal administering a plasmid vector (a nucleic acid molecule free of an infectious agent) to mucosal tissue of mice, wherein the plasmid contains a DNA sequence encoding an influenza viral antigen operatively linked to a CMV promoter (regulatory sequence), which induced a humoral immune response (column 32, line 54 to column 33, line 14), and cellular immune response including antigen specific cytotoxic T Lymphocytes (examples XII-XIV). *Carson et al* teach that the mucosal routes of administration can be nasal, rectal, vaginal, urethra, or mouth topically (column 6, lines 21-27), and the principle is to deliver the naked DNA to areas rich in APC, such as the squamous buccal mucosal epithelia (column 6, lines 2-5). *Carson et al* also teach suppository and topical preparations are suitable for mucosal administration (column 20, lines 1 1-19). *Carson et al* go on to teach that immunostimulatory *cytokine* could be co-administered with polynucleotide expressing an antigen to enhance the performance of the host immune system, particularly the helper and cytotoxic T lymphocytes (e.g. paragraph bridging columns 29-30). *Carson et al* do not mention "sublingual" mucosa in the '647 patent. However, long before the effective filing date, *Harris et al* discuss drug delivery via the mucosal tissue of the

mouth (oral cavity). *Harris et al* teach the mucous membrane lining of the oral cavity comprises sublingual and buccal mucosa, which differs in anatomy, permeability to an applied drug, and the ability to retain a delivery system. *Harris et al* teach it is widely accepted that the sublingual route is relatively permeable, giving rapid absorption and acceptable bioavailabilityies, whereas buccal route may be more advantageous under certain conditions such as peptide drug delivery (e.g. table I). Apparently, the skilled in the art acknowledges the term "mouth" encompasses both "buccal and sublingual" mucosa, the differences between the two sites are well-defined and so does the reasoning for using such in drug delivery. *Carson et al* do not teach using IL-12 as the immunostimulatory molecule.

Gately et al supplemented the teaching of *Carson et al* by establishing that it is well known in the art that IL-12 is a cytokine that could enhance the performance of activated T lymphocytes and natural killer cells, which are immune cells particularly relevant to host defense against pathogens such as viruses. *Gately et al* teach that IL-12 could stimulate LAK cells as well as CTL responses, thus useful as a therapeutic agent against tumors and infectious diseases (e.g. abstract and introduction).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Carson et al* with that of *Gately et al* by simply selecting one of the art known routes of antigen administration, such as buccal or sublingual for vaccination and including IL-12 in the vaccine composition with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention because in light of

numerous art known mucosal delivery routes and immunostimulatory cytokines, these limitations would fall within the bounds of the optimization. Further, given the success disclosed in the individual references, the reasonable skilled would have had a reasonable expectation of success when use them combined. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 42, 43, 48, 49, 52, 53, 90, 91, 96, 97, 102, 103 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Carson et al* (US 5,679,647), and *Gately et al* (Cell Immunol 1992;143:127-42) as applied to claims 15, 16, 39-41, 45-47, 51, 81, 83, 85, 87, 89, 93, 95, 99, 101, 108-114 above, further in view of *Wang et al* (PNAS 1993;90:4156-60).

The teachings of *Carson et al* and *Gately et al* disclosed a method for inducing immune response against a viral antigen, preferably combined with an immunostimulatory cytokine such as IL-12 as discussed in detail above. However, the combined teachings do not specifically define that the antigen is from human immunodeficiency virus, preferably comprises an epitope of gp160.

Wang et al supplemented the teachings of *Carson et al* and *Gately et al* by establishing that HIV gp160 is a known vaccine antigen in the art at the time of instant filing date. *Wang et al* teach administering a plasmid encoding an HIV gp160 as vaccine for HIV infection, and induced both humoral and cellular immune response via intramuscular injection. *Wang et al* do not teach the mucosal route of administration.

However, *Carson et al* teach the advantage of using mucosal administration over intramuscular administration, "ROUTES OF ADMINISTRATION OF NAKED POLYNUCLEOTIDES THROUGH SKIN OR MUCOSA REQUIRE A LOWER CONCENTRATION OF DNA TO PRODUCE THE SAME MAGNITUDE OF IMMUNE RESPONSE THAN DOES THE INTRAMUSCULAR ROUTE OF ADMINISTRATION", and this is particularly desirable when using the DNA introducing a foreign antigen (column 8, lines 30-44).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the methods taught by *Carson et al, Gately et al,* and *Wang et al* for developing vaccine against an antigen of interest such as the HIVgp160 with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention because the mucosal route requires less amount of antigen for inducing an effective immune response and it is within the knowledge of the skill to select the antigen of interest for vaccination. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claim Objections

Claims 44, 50, 54, 82, 84, 86, 88, 94, 98, 100, 104, 105-107 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Dave T. Nguyen** can be reached on 571-272-0731. The **fax** numbers for the organization where this application or proceeding is assigned are **571-273-8300**.

Any inquiry of formal matters can be directed to the patent analyst, **Victor Barlow**, whose telephone number is (571) 272-0506.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Q. JANICE LI, M.D.
PRIMARY EXAMINER

Q. Janice Li, M.D.
Primary Examiner
Art Unit 1633

QJL
November 9, 2005